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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/500,613	11/16/2004	William A Carter	51-575	7887

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EXAMINER	
GIBBS, TERRA C	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 10/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/500,613	CARTER ET AL.	
	Examiner	Art Unit	
	Terra C. Gibbs	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *June 14, 2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is a response to Applicant's Preliminary Amendment filed June 14, 2004.

Claims 1-3, 5, and 7 have been amended.

Claims 1-7 are pending in the instant application.

Claims 1-7 have been examined on the merits.

Priority

Applicant's reference to priority in the first sentence of the specification is acknowledged. It is noted that Applicant has filed a certified copy of the Foreign Application as required by 35 U.S.C. §119(a) -(e).

Information Disclosure Statement

Applicant's information disclosure statement filed June 14, 2004 is acknowledged. The submission is in compliance with the provisions of 37 CFR §1.97. Accordingly, the Examiner has considered the information disclosure statement, and a signed copy is enclosed herewith.

Claim Objections

Claim 2 is objected to because of the following informalities:

Claim 2 contains a typographical error since it appears that the first word of the claim "he" should be correctly spelled as "The". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2, 3, 5, and 6 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 is indefinite because it recites the phrase, "wherein step a dsRNA". This phrase is grammatically incorrect. Removal of the word "step" in the claim would overcome the instant rejection.

Claim 3 is indefinite because it recites the phrase, "wherein step HIV". This phrase is grammatically incorrect. Removal of the word "step" in the claim would overcome the instant rejection.

Claim 5 is indefinite because the preamble recites, "The claim 1". This preamble is grammatically incorrect. Replacement with the preamble, "The method of claim 1" in this claim would overcome the instant rejection.

Claim 6 is indefinite because the preamble recites, "The method of claim 5". There is insufficient antecedent basis for this limitation in the claim because claim 5 is grammatically incorrect and does not recite a method. Also, claim 6 is indefinite because it recites the phrase, "wherein the anti-retroviral drug". There is insufficient antecedent basis for this limitation in the claim because claim 5, from which claim 6 depends, recites the term, "anti-retroviral agent". Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Carter, WA [U.S. Patent No. 4,950,652] ('652), made of record on Applicant's information disclosure statement filed June 14, 2004.

Claim 1 is drawn to a method of mitigating the adverse effects of antiviral agents in HIV therapy comprising administering to an HIV-infected subject at least one antiviral agent until HIV is suppressed, discontinuing antiviral therapy, administering a dsRNA, then, when HIV values increase, resuming antiviral treatment with at least one antiviral agent. Claims 2 and 7 depend from claim 1 and include all the limitations of claim 1 with the further limitations wherein the dsRNA is administered with said antiviral agent, and wherein the dsRNA is $rI_n\ r(C_{12}U)_n$, Poly A Poly U or $rI_n\ r(C_{29}G)_n$, in which r is ribo and n has a value of 4 to 29.

'652 discloses and claims a method of treating retroviral disease in a person having HIV comprising administering an antiviral agent in combination with a dsRNA (see Abstract, column 1, lines 57-60, column 2, lines 45-52, column 3, lines 1-4, and claims 4 and 7). '652 also discloses and claims that the dsRNAs are mismatched analogs of complexes of polyriboinosinic and polyribocytydilic acids of the formula $rI_n\ r(C_{11\text{-}14}U)_n$ and $rI_n\ r(C_{29}G)_n$ (see column 3, lines 33-50, and claim 4). It is noted that '652

discloses that antiviral drugs were administered alone or in combination with dsRNA (see column 1, lines 57-60 and column 3, lines 1-4).

It is noted that '652 is silent regarding the sequential order of treatment of HIV with the antiviral agent in combination with the dsRNA. However, the burden of establishing whether the prior art method discontinued antiviral therapy then resumed antiviral treatment falls to Applicant. See MPEP 2112.01, "Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the prima facie case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. In re Best, 562 F.2d at 1255, 195 USPQ at 433." See also MPEP 2112: "[T]he PTO can require an Applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [her] claimed product." The MPEP at 2112 citing *In re Fitzgerald* 205 USPQ 594. 596, (CCPA 1980), quoting In re Best 195 USPQ 430 as per above. Therefore, it falls to Applicant to determine and provide evidence that the method of treatment of HIV with the antiviral agent in combination with the dsRNA disclosed by '652 was discontinued and then resumed, at any point, as claimed. Therefore, absent evidence to the contrary, claims

1, 2, 5, and 7 are anticipated by '652.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Carter, WA [U.S. Patent No. 4,950,652] ('652), (made of record on Applicant's information disclosure statement filed June 14, 2004), in view of Ruiz et al. (AIDS, 2001 Vol. 15:F19-F27, made of record on Applicant's information disclosure statement filed June 14, 2004), and Schlomo et al. (JAMA, 2001 Vol. 285:1155-1163).

Claim 1 is drawn to a method of mitigating the adverse effects of antiviral agents in HIV therapy comprising administering to an HIV-infected subject at least one antiviral agent until HIV is suppressed, discontinuing antiviral therapy, administering a dsRNA, then, when HIV values increase, resuming antiviral treatment with at least one antiviral agent. Claims 2-7 depend from claim 1 and include all the limitations of claim 1 with the

further limitations wherein the dsRNA is administered with said antiviral agent; wherein HIV values are suppressed to a value below detection; wherein the value is less than 50 copies/ml of HIV plasma RNA; wherein two or more anti-retroviral agents are used; wherein the anti-retroviral agent is selected from abacavir, amprenavir, zidovudine, combivir, zalcitabine, lamivudine, didanosine, trizivir, stavudine, lopinavir, efavirenze, nevirapine, indinavir, delavirdine, ritonavir, saquinavir, nelfinvir, and tenofovir, and wherein the dsRNA is $rI_n\ r(C_{12}U)_n$, Poly A Poly U or $rI_n\ r(C_{29}G)_n$, in which r is ribo and n has a value of 4 to 29.

'652 teaches and claims a method of treating retroviral disease in a person having HIV comprising administering an antiviral agent in combination with a dsRNA (see Abstract, column 1, lines 57-60, column 2, lines 45-52, column 3, lines 1-4, and claims 4 and 7). '652 also teaches and claims that the dsRNAs are mismatched analogs of complexes of polyriboinosinic and polyribocytydilic acids of the formula $rI_n\ r(C_{11\text{-}14}U)_n$ and $rI_n\ r(C_{29}G)_n$ (see column 3, lines 33-50, and claim 4). It is noted that '652 teaches that antiviral drugs were administered alone or in combination with dsRNA (see column 1, lines 57-60 and column 3, lines 1-4).

It is noted that '652 is silent regarding the sequential order of treatment of HIV with the antiviral agent in combination with the dsRNA. However, the burden of establishing whether the prior art method discontinued antiviral therapy then resumed antiviral treatment falls to Applicant. See MPEP 2112.01, "Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either

anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the prima facie case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. In re Best, 562 F.2d at 1255, 195 USPQ at 433." See also MPEP 2112: "[T]he PTO can require an Applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [her] claimed product." The MPEP at 2112 citing *In re Fitzgerald* 205 USPQ 594. 596, (CCPA 1980), quoting In re Best 195 USPQ 430 as per above. Therefore, it falls to Applicant to determine and provide evidence that the method of treatment of HIV with the antiviral agent in combination with the dsRNA taught by '652 was discontinued and then resumed, at any point, as claimed.

'652 does not teach wherein HIV values are suppressed to a value below detection, wherein the value is less than 50 copies/ml of HIV plasma RNA, wherein two or more anti-retroviral agents are used, or wherein the anti-retroviral agent is selected from abacavir, amprenavir, zidovudine, combivir, zalcitabine, lamivudine, didanosine, trizivir, stavudine, lopinavir, efavirenze, nevirapine, indinavir, delavirdine, ritonavir, saquinavir, nelfinvir, and tenofovir.

Schlomo et al. teaches a triple combination therapy of abacavir, lamivudine, and zidovudine or indinavir, lamivudine, and zidovudine in antiretroviral-naïve HIV-infected

adults (see Context). Specifically, Schlomo et al. teach some patients administered with the abacavir, lamivudine, and zidovudine regimen and some patients administered with the indinavir, lamivudine, and zidovudine regimen exhibited less than 50 copies/ml of HIV plasma RNA (see Figure 2C).

It would have been obvious to one of ordinary skill in the art to devise a method of mitigating the adverse effects of antiviral agents in HIV therapy comprising administering to an HIV-infected subject at least one antiviral agent until HIV is suppressed, discontinuing antiviral therapy, administering a dsRNA, then, when HIV values increase, resuming antiviral treatment with at least one antiviral agent using the teachings of '652.

One of ordinary skill in the art would have been motivated to discontinue therapy and then resume therapy since Ruiz et al. taught that treatment interruptions boost immunity and limit virus replication (see Results). One of ordinary skill in the art would have been motivated to administer the dsRNA with the antiviral agent since '652 taught that certain combination antiviral therapies exhibit synergistic effects. One of ordinary skill in the art would have been motivated to achieve less than 50 copies/ml of HIV plasma because it is well known in the art that this value is considered to indicate a more durable virologic response, indicating successful HIV treatment (see Ruiz et al. at page 1161, last column). One of ordinary skill in the art would have been motivated to combine two or more anti-retroviral agents in combination with a dsRNA for HIV treatment since the prior art taught combination therapy results in less than 50 copies/ml of HIV plasma RNA, indicating successful HIV treatment.

One of ordinary skill in the art would have expected success at devising a method of mitigating the adverse effects of antiviral agents in HIV therapy comprising administering to an HIV-infected subject at least one antiviral agent until HIV is suppressed, discontinuing antiviral therapy, administering a dsRNA, then, when HIV values increase, resuming antiviral treatment with at least one antiviral agent since '652 explicitly taught the success of such a method. One of ordinary skill in the art would have expected success at using two or more anti-retroviral agents and achieving less than 50 copies/ml of HIV plasma since Ruiz et al. taught the successful use of triple combination regimens in treating HIV-infected patients.

Therefore, the invention would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Terra C. Gibbs whose telephone number is 571-272-0758. The examiner can normally be reached on 9 am - 5 pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

tcg
September 27, 2006